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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FOLEY, SHANON A	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/766,344	PARKIN ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *122-150* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *122-150* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

The request filed on for a Request for Continued Examination (RCE) under 37 CFR §1.114 based on parent Application No. 09/766344 is acceptable and a RCE has been established. An action on the RCE follows.

In the amendment submitted November 14, 2003, applicant cancelled claims 98-112, 114-117 and 121 and added new claims 122-150. Claims 122-150 are under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 122-150 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claimed method of assessment in claims 122, 126, 127, 138, 139 and 149 does not have a clear point that ties to assessing the effectiveness of the antiviral therapy. The claimed method determines whether a patient has mutations in an HIV protease relative to a reference HIV protease. The steps required for this determination do not address the effectiveness of the protease therapy that is stated in the preamble of the claims. On page 2 of the specification, there is a discussion about making choices regarding initial and subsequent therapies based on resistance patterns. Incorporating this concept into the claims would provide an active step for determining antiviral therapy. To obviate this rejection, applicant should incorporate language into the claims that states that the specific protease treatment is discontinued if the mutation is

present and that the specific protease treatment is continued if the mutation is absent. This rejection affects all dependent claims.

There is a direct discrepancy in the subject matter claimed in claims 131-137 and claims 139-149. In the first set of claims, detection of certain mutations indicates a decrease in susceptibility to saquinavir and/or indinavir, while in the second set of claims, detection of the same mutations indicates an increase in susceptibility to saquinavir and/or indinavir. It is not clear how detection of the same mutations infers the opposite determination of susceptibility for the same drugs.

Claims 124, 130-134, 136, 137, 142-145 and 148 recite the limitation "nucleic acid" in line 1. There is insufficient antecedent basis for this limitation in the claims.

Claim 125 recites the limitation "said difference" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 147 recites the limitation "said increase" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 150 states that the amount of expression of the indicator gene depends on the activity of the HIV protease. It is not clear what the nexus is between protease activity and the indicator gene. What is the indicator gene indicating? What would be affecting the activity of the HIV protease? How is the amount of expression of the indicator gene determined?

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 122-130 and 138 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting a decrease in drug susceptibility by determining the presence of the claimed mutations, does not reasonably provide enablement for detecting an increase in drug susceptibility by detecting the presence of the claimed mutations. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a method of assessing the effectiveness of protease antiviral therapy by determining whether a patient sample comprises primary mutations at codons 82 or 90 and selected secondary mutations. The claims specify that the presence of the mutations indicates a difference in the HIV protease's susceptibility to amprenavir, indinavir and/or saquinavir. The prior art indicates that mutations at codon positions 82 and/or 90, along with some of the secondary codons claimed, indicates increased drug resistance to indinavir and/or saquinavir, among other drugs, see the Table 1 of Young et al. (Journal of Infectious Diseases. 1998; 178: 1497-1501) for example. The working examples, throughout pages 106-189, indicates that mutations found within codons 82 and/or 90, along with secondary mutations, correlated with a decrease in susceptibility for amprenavir, indinavir, saquinavir and/or other protease inhibitors. Therefore, due to the working examples and the prior art, clearly indicating that mutations at codons within the HIV protease during protease inhibitor therapy correlate with a decrease in drug susceptibility, it is determined that the claims require an undue quantity of experimentation to detect an increase to susceptibility to protease inhibitor drugs commensurate in scope with the claims.

Claims 139-149 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a method of assessing the effectiveness of protease therapy by determining the presence of mutations at codons 82 and/or 90 with secondary mutations. The claims state that the presence of these mutations indicate an increase in the HIV protease's susceptibility to protease inhibitor therapy. However, as discussed above, the instant working examples on pages 106-189 and the teachings of Young et al. state that the presence of the mutations recited in the claims result in an increase in drug resistance, i.e. an decrease in susceptibility. Therefore, it is determined that an undue quantity of experimentation would be required of the skilled artisan to make and/or use the method to determine an increase in protease inhibitor therapy by detecting the presence of the instant mutations.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 122-135, 137 and 138 are rejected under 35 U.S.C. 102(b) as being anticipated by Craig et al. (AIDS. 1998; 12: 1611-1618).

Claims 122-126 are drawn to a method of assessing the effectiveness of protease antiviral therapy by detecting a nucleic acid encoding an HIV protease that comprises a mutation at codon

82 or 90 and specified secondary mutations. The presence of the mutations indicates a difference in the HIV protease's susceptibility to amprenavir. Claims 127-135, 137 and 138 are drawn to same method, wherein the presence of the mutations indicates a difference in the HIV protease's susceptibility to any protease inhibitor, but especially indinavir, amprenavir or saquinavir.

Craig et al. teach a method of assessing the effectiveness of antiviral protease inhibitor therapy by detecting mutations in HIV protease from patients. Craig et al. teach that the presence of a mutations at codons 90, 73, 71, 93, 46, 84, 48, 82, 72, 54 and 20 result in a reduced sensitivity to saquinavir, indinavir, ritonavir, amprenavir and nelfinavir, see Table 2 on page 1615. Craig et al. also teach mutations at codons 82, 73, 48, 90, 36 and 84 result in a reduced sensitivity to saquinavir, indinavir, ritonavir, amprenavir and nelfinavir, see Table 2 on page 1615. Craig also anticipate the specific codon substitutions recited in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 150 is rejected under 35 U.S.C. 103(a) as being unpatentable over Craig et al. and Capon et al. (US 5,837,464).

The claim is drawn to a test vector comprising a protease-encoding segment from an HIV-infected patient comprising certain mutations and an indicator gene.

See the teachings of Craig et al. above. Craig et al. do not teach a test vector with an indicator gene.

However, Capon et al. does, see claims 30-34, 37, 38, 45-47. One of ordinary skill in the art at the time the invention was made would have been motivated to express the patient-derived segment of Craig et al. into the resistance test vector of Capon et al. to amplify genes that contain possible drug-resistant mutations so as not to deplete the primary source derived directly from the patient. One of ordinary skill would be further motivated to express patient-derived segments into a test vector to simultaneously test different segments that may not be adjacent in the genome and spare the time and expense of generating recombinant viruses expressing mutations. One of ordinary skill in the art at the time the invention was made would have also been motivated to express patient-derived segments in an expression vector to evaluate the effect of the patient-derived segment with other protease drug candidates. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation in producing the claimed invention because Capon et al. teaches introducing the test vector into host cells to determine drug resistance mutations, see claim 46, and Craig et al. teach determining the presence of drug resistance by transforming recombinant viruses in tissue culture in the presence of drugs, see the Materials and Methods section bridging pages 1612-1613. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley

Patent Examiner, 1600